QUESTION 1

What is your status?

1. Staff Radiation Oncologist

2. Resident Radiation Oncologist 1st yr

3. Resident Radiation Oncologist 2nd yr

4. Resident Radiation Oncologist 3rd yr

5. Other professionals
QUESTION 2

How confident are you for treatment of PC with hormonal therapy?

score 1-10

1 for minimal “I am not confident at all”

10 for maximal “I am very confident”
WHY HORMONAL TX FOR PC

• Androgens promote the growth of both normal and cancerous prostate cells by binding to and activating the androgen receptor, a protein that is expressed in prostate cells.

• Once activated, the androgen receptor stimulates the expression of specific genes that cause prostate cells to grow.

• Treatments that decrease androgen levels or block androgen activity can inhibit their growth.
Concepts of hormonal therapy

“Testosterone (T) and the intracellular metabolite dihydrotestosterone (DHT) w/ 10 times potency are the primary substances responsible for prostate growth and maintenance”

“If prostate cells are deprived of androgen stimulation, they undergo apoptosis (programmed cell death)”
TYPES OF HORMONAL TX

1. Reduce androgen production by the testicles
2. Block the action of androgens in the body
3. Block the production of androgens from adrenal gland
REduce ANDROGEN PRODUCTION BY THE TESTICLES

Bilateral Orchiectomy (surgical castration)

✧ reduce testosterone level 90-95%

✧ permanently
REDUCE ANDROGEN PRODUCTION BY THE TESTICLES

Medical castration

• reduce testosterone level by 90-95%

• reversible

  LHRH/GnRH agonist

  LHRH/GnRH antagonist
LHRH/GnRH agonist

- LHRH agonists (LHRH analogs), are synthetic proteins structurally similar to LHRH / Bind to the LHRH receptor in pituitary gland.

- LHRH, initially stimulate production of luteinizing hormone (LH). However, the continued presence of high levels of LHRH agonists causes the pituitary gland to stop producing LH, which prevents testosterone from being produced.
LHRH/GnRH agonist

• When pts received LHRH agonist first time, they may experience "testosterone flare."

• This temporary increase in testosterone level occurs because LHRH agonists briefly cause the pituitary gland to secrete extra LH before blocking its release.

• The flare may worsen clinical symptoms (e.g. bone pain, ureter or bladder outlet obstruction, and spinal cord compression)

• Countered by giving antiandrogen therapy along with an LHRH agonist for the first few weeks of treatment.
Which one is **NOT** LHRH agonist?

1. Goserelin
2. Leuprolide
3. Degarelix
4. Triptorelin
# LHRH/GnRH agonist in Thailand

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade name</th>
<th>Form</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Goserelin</strong></td>
<td>Zoladex™</td>
<td>SC implant</td>
<td>3.6 mg q 1 mo&lt;br&gt;10.8 mg q 3 mo</td>
</tr>
<tr>
<td><strong>Leuproline</strong></td>
<td>Enantone™</td>
<td>IM, SC</td>
<td>3.75 mg q 1 mo&lt;br&gt;11.25 mg q 3 mo</td>
</tr>
<tr>
<td></td>
<td>Eligard™</td>
<td>IM, SC</td>
<td>7.5 mg q 1 mo&lt;br&gt;22.5 mg q 3 mo</td>
</tr>
<tr>
<td><strong>Triptorelin</strong></td>
<td>Dipherelatin™</td>
<td>IM, SC</td>
<td>3.75 mg q 1 mo&lt;br&gt;11.25 mg q 3 mo</td>
</tr>
</tbody>
</table>
Goserelin (Zoladex)
Leuprololne (Enantone)
Leuproline (Eligard)
Triptorelin (Dipherelin)
LHRH/GnRT agonist
Common Side Effects

- Loss of libido and erectile dysfunction
- Hot flushes- most common and could be long term
- Depressive mood
- Osteoporosis
- Obesity and Muscle loss- occur early in first year
- Precipitate DM and hyperlipidemia
- Increase risk of CVD, MI (even w/ short term H)
- decreased testicle size
- rash, itching, allergic reaction
- redness, pain, swelling, or oozing where the shot was given.
LHRH/GnRH Antagonist

- LHRH antagonists act by preventing LHRH from binding to its receptors in the pituitary gland.
- Prevents secretion of LH, causing the body’s androgen levels to drop.
- Unlike LHRH agonists, LHRH antagonists do not cause a testosterone flare.
- One LHRH antagonist, Degarelix (Firmagon™), is currently approved to treat advanced prostate cancer.
## Degarelix (Firmagon™)

<table>
<thead>
<tr>
<th>Starting dose</th>
<th>Maintenance dose – Administration every 28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>240 mg given as two subcutaneous injections of 120 mg at a concentration of 40 mg/mL</td>
<td>80 mg given as one subcutaneous injection at a concentration of 20 mg/mL</td>
</tr>
</tbody>
</table>
Aim of medical castration

- Testosterone < 50 ng/ml
- Recently recommend of castrate level; Testosterone < 20 ng/ml
TYPES OF HORMONAL TX

1. Reduce androgen production by the testicles

2. Block the action of androgens in the body

3. Block the production of androgens from adrenal gland
Block the action of androgens in the body

Function: compete with testosterone and DHT at the receptor level in the prostate cell nucleus

Results: Promoting apoptosis and inhibition of prostate cancer growth
Block the action of androgens in the body

- Because **antiandrogens** do not block androgen production, they rarely used on their own to treat prostate cancer.

- They are used in combination with orchiectomy or an LHRH agonist.

- Use antiandrogen drug in combination with orchiectomy or an LHRH agonist is called **combined androgen blockade (CAB)**, complete androgen blockade, or total androgen blockade.
QUESTION 4

Which one is **NOT** antiandrogen?

1. Cypoterone
2. Abiraterone
3. Flutamide
4. Bicalutamide
Anti-androgens in Thailand (Pills)

Steroidal anti-androgens:
- Cyproterone (Androcur™)
- Megestral acetate (Megace™, Megaplex™)/Medroxyprogesterone acetate (Farlutal™)

Non-steroidal anti-androgens:
- Flutamide (Flutan™, Fugerel™)
- Bicalutamide (Casodex™, Calumid™)
- Enzalutamide (Xtandi™)
TYPES OF HORMONAL TX

1. Reduce androgen production by the testicles

2. Block the action of androgens in the body

3. Block the production of androgens from adrenal gland
Block the production of androgens from adrenal gland/Body

- Drugs that prevent the adrenal glands (as well as the testicles and prostate cancer cells) from making androgens are called **androgen synthesis inhibitors**

- These drugs block testosterone production by inhibiting an enzyme called CYP17. This enzyme plays a central role in allowing the body to produce testosterone from cholesterol.
Androgen synthesis inhibitors in Thailand (Pills)

- ketoconazole is approved for indications other than prostate cancer but are sometimes used as second-line treatments for castration-resistant prostate cancer.

- abiraterone acetate, is approved to treat metastatic castration-resistant prostate cancer.
GUIDELINE STATEMENTS

Definitive Treatment for Low-Risk Prostate Cancer

- Clinicians should not add ADT along with radiotherapy except to reduce prostate size for brachytherapy (Strong Recommendation; Evidence Level B)
- Clinicians should inform patients considering cryosurgery that side effects are considerable and survival benefit has not been shown compared to active surveillance (Conditional Recommendation; Evidence Level C)
- Clinicians should inform patients who are considering focal therapy or HIFU that these interventions are not standard care options because comparative outcome evidence is lacking (Expert Opinion/No RCT evidence)
GUIDELINE STATEMENTS

Standard Treatment Option

• Clinicians should recommend radical prostatectomy or radiotherapy plus androgen deprivation therapy (ADT) as standard treatment options for patients with intermediate-risk localized prostate cancer (Strong Recommendation; Evidence Level A)

Alternative Options

• Clinicians should inform patients that favorable intermediate-risk prostate cancer can be treated with radiation alone, but that the evidence basis is less robust than for combining radiotherapy with ADT (Moderate Recommendation; Evidence Level B)
Standard Therapy

- Clinicians should recommend radical prostatectomy or radiotherapy plus ADT as standard treatment options for patients with high-risk localized prostate cancer (*Strong Recommendation, Evidence Level A*)
Prostate cancer & Hormonal Tx

High-grade PIN

Localised prostate cancer

Locally advanced

Metastatic disease

Hormone insensitive

Treatment options:

Radical prostatectomy
RT alone for Low risk
RT + HT for interm. risk
Active surveillance

Hormonal therapy

Chemotherapy
continue castration

Radiotherapy + HT
Hormonal therapy
‘Watchful waiting’

Time (years)
Inclusion criteria

or older, with histologically confirmed adenocarcinoma of the prostate, stage pT2, pT3, and pT4a (bladder neck involvement only), and pN0 or pNx, who had received radical prostatectomy. No systematic tests were done to assess testosterone recovery after hormonal treatment. Eligible patients had PSA concentrations of less than 0.1 μg/L for at least 6 months after surgery, which then began to rise (to between 0.2 μg/L and <2 μg/L, as confirmed by two consecutive tests) without evidence of

Exclusion criteria

known pituitary adenoma. Patients were excluded if they had undergone previous androgen deprivation therapy or pelvic radiotherapy, if the initial status at the time of surgery was pN1, if histology findings showed cancer other than adenocarcinoma, if the patient had
Study design

- Randomized, open-label, multicenter phase III study
- Stratification criteria
  - Investigational site
  - IMRT vs 3D RT
  - High risk vs low risk

Low risk (of DM)
Gleason score <8
and positive surgical margins
and PSA doubling time at relapse > 6 months
and no seminal vesicle involvement
Salvage radiotherapy with or without short-term hormone therapy for rising prostate-specific antigen concentration after radical prostatectomy (GETUG-AFU 16): a randomised, multicentre, open-label phase 3 trial

80%: RT+ADT (363pts)

62%: RT (367pts)

p < 0.0001

Figure 2: Kaplan-Meier estimates of progression-free survival
Subgroups analysis

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>N&lt;sub&gt;RT&lt;/sub&gt; / N&lt;sub&gt;RT+ADT&lt;/sub&gt;</th>
<th>HR</th>
<th>CI (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>115 / 106</td>
<td>0.40</td>
<td>(0.20 - 0.77)</td>
</tr>
<tr>
<td>High risk</td>
<td>258 / 263</td>
<td>0.51</td>
<td>(0.38 - 0.70)</td>
</tr>
<tr>
<td>3D RT</td>
<td>355 / 354</td>
<td>0.50</td>
<td>(0.38 - 0.67)</td>
</tr>
<tr>
<td>IMRT</td>
<td>18 / 15</td>
<td>0.40</td>
<td>(0.08 - 2.08)</td>
</tr>
<tr>
<td>PSA ≤ 0.5</td>
<td>305 / 284</td>
<td>0.55</td>
<td>(0.39 - 0.77)</td>
</tr>
<tr>
<td>PSA &gt; 0.5</td>
<td>66 / 83</td>
<td>0.32</td>
<td>(0.19 - 0.53)</td>
</tr>
<tr>
<td>PSA ≤ 1</td>
<td>345 / 346</td>
<td>0.50</td>
<td>(0.37 - 0.68)</td>
</tr>
<tr>
<td>PSA &gt; 1</td>
<td>26 / 21</td>
<td>0.46</td>
<td>(0.20 - 1.09)</td>
</tr>
<tr>
<td>PSA -DT &gt; 6 months</td>
<td>276 / 270</td>
<td>0.53</td>
<td>(0.38 - 0.75)</td>
</tr>
<tr>
<td>PSA =DT ≤ 6 months</td>
<td>97 / 99</td>
<td>0.42</td>
<td>(0.26 - 0.68)</td>
</tr>
<tr>
<td>All population</td>
<td>373 / 369</td>
<td>0.50</td>
<td>(0.38 - 0.66)</td>
</tr>
</tbody>
</table>
Overall Survival

- Stratified Log-rank test: $p = 0.1849$

<table>
<thead>
<tr>
<th></th>
<th>RT</th>
<th>RT + ADT</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>373</td>
<td>369</td>
</tr>
<tr>
<td>Deaths</td>
<td>26 (7.0%)</td>
<td>17 (4.6%)</td>
</tr>
<tr>
<td>5-year OS rate [95% CI]</td>
<td>94.8% [92-97]</td>
<td>96.2% [93-98]</td>
</tr>
<tr>
<td>HR [95% CI]</td>
<td>0.66 [0.36 - 1.22]</td>
<td></td>
</tr>
</tbody>
</table>
### Future study

<table>
<thead>
<tr>
<th>Early RT</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Salvage RT</td>
<td></td>
</tr>
<tr>
<td>Radiotherapy Alone</td>
<td>Drug: bicalutamide</td>
</tr>
<tr>
<td>Radiotherapy + 6 months</td>
<td>Drug: goserelin acetate</td>
</tr>
<tr>
<td>Radiotherapy + 24 months</td>
<td>Drug: leuprolide acetate</td>
</tr>
</tbody>
</table>

**Enrollment:** 4236  
**Study Start Date:** November 2007  
**Estimated Study Completion Date:** September 2021
Future study

❖ GETUG-17 study

Estimated Enrollment: 718
Study Start Date: December 2007
Estimated Primary Completion Date: December 2022

❖ Arm 1: Delay RT, Triptorelin
PSA at start RT >0.2 - < 2 ng/mL

❖ Arm 2: Immediate RT, Tx as arm 1, Tx begins within 6 mo after RP
<table>
<thead>
<tr>
<th>Type</th>
<th>Generic Name</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Androgen</td>
<td>Flutamide 250 mg PO Tid</td>
<td>biochemical failure after castration until progression</td>
</tr>
<tr>
<td></td>
<td>Bicalutamide 50 mg PO OD</td>
<td>biochemical failure after castration until progression</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>800-1,200 mg/day</td>
<td>Castration resistant Prostate cancer until progression</td>
</tr>
<tr>
<td>LHRH agonist</td>
<td>Leuprolelin DPS 11.25 mg (Enantone)</td>
<td>adjuvant therapy ร่วมกับการให้รังสีรักษา เพื่อรักษาผู้ป่วยมะเร็งต่อมลูกหมากในผู้ป่วยที่แบ่งกลุ่มระดับความเสี่ยงกลาง (Intermediate risk) ความเสี่ยงสูงและสูงมาก (High risk and very high risk)</td>
</tr>
<tr>
<td></td>
<td>Leuprolelin vial 22.5 mg (Eligard)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Triporelin vial 11.25 mg (Diphereline)</td>
<td></td>
</tr>
</tbody>
</table>
การใช้ LHRH agonists ไนสิทธิ์ สบสช. ปีงบประมาณ 2561

มีข้อบ่งชี้ในการนี้

• ข้อบ่งชี้ ใช้เป็น adjuvant therapy ร่วมกับการให้รังสีรักษาให้รังสีรักษาในกลุ่มผู้ป่วยมะเร็งต่อมลูกหมาก intermediate risk คือผู้ที่อยู่ในระยะโรค cT2b ถึง cT2c ตาม TNM staging system หรือมีค่า Gleason score เท่ากับ 7 หรือมีค่า serum PSA เท่ากับ 10-20 ng/ml อย่างใดอย่างหนึ่ง. ให้ LHRH agonist ตามรายการ ไม่เกิน 2 cycles

• ข้อบ่งชี้ ใช้เป็น adjuvant therapy ร่วมกับการให้รังสีรักษาให้รังสีรักษาในกลุ่มผู้ป่วยมะเร็งต่อมลูกหมาก High risk of recurrence คือผู้ที่อยู่ในระยะโรค cT3a ตาม TNM staging system หรือมีค่า Gleason score เท่ากับ 8-10 หรือมีค่า serum PSA มากกว่า 20 ng/ml อย่างใดอย่างหนึ่ง หรือผู้ป่วยอยู่ในกลุ่มผู้ป่วยมีความเสี่ยงสูงมาก (Very high risk of recurrence) คือผู้ที่อยู่ในระยะโรค cT3b ถึง cT4 ให้ LHRH agonist ตามรายการ ไม่เกิน 8 cycles
การใช้ Hormonal Tx ไปสิทธิ์อื่นๆ

ยาในบัญชียาหลักแห่งชาติ

- Flutamide
- Ketoconazole

ยานอกบัญชียาหลักแห่งชาติ

- All LHRH Agonist/ Antagonist ซึ่งทะเบียนเรื่องมะเร็งต่อมลูกหมาก แต่ที่มีการใช้ร่วมกับ Radiation คือ Zoladex/ Enantone
- Megace ไม่ได้ขึ้นทะเบียนเรื่องมะเร็งต่อมลูกหมาก
- Farlutal
- Bicalutamide
- Enzalutamide
- Abiraterone
QUESTION 5

How confident you are for treatment of PC with hormonal therapy?

score 1-10

1 for minimal “I am not confident at all”

10 for maximal “I am very confident”
Case Discussion
Case 1

- 51 year old, healthy man
  - PSA 2.1 in 2001
  - PSA 2.4 in 2002
  - PSA 5.3 in 2003

- Biopsy (gland volume 25 cc)
  - 4/6 cores 3+4 =7 (Rt mid and base)
  - 2/6 cores 4+3 =7 (Lt base)

- DRE: 0.5 cm firm nodule at Rt lobe
According to NCCN risk stratification, which risk group is this pt?

1. Low risk
2. Intermediate risk
3. High risk
Case 1

**QUESTION 7**

What treatment would you recommend for this patient?

1. Active Surveillance
2. Radical prostatectomy
3. Radiation therapy
4. Radiation + short term Hormonal treatment
5. Radiation + long term Hormonal treatment
Case 1

- This patient was treated by left sided nerve sparing RP 6/1/03
- Patho: Adenocarcinoma GS 4+3
  ECE+ at right base
  Distal SM +
  No seminal vesicle involvement
  LN 0/4
Case 1

Should the patient be offered post operative RT?

1. Yes
2. No
Case 1

- **Post op PSA levels**
  - 7/03: <0.1
  - 7/04: 0.07
  - 10/04: 0.4
  - 4/05: 0.8
  - 10/05: 1.6
Case 1

- When do you consider this case PSA failure?
  1. 7/03  PSA  <0.1
  2. 7/04  PSA  0.07
  3. 10/04 PSA  0.4
  4. 4/05 PSA  0.8
  5. 10/05 PSA  1.6
Case 1

- Post op PSA levels
  - 7/03 <0.1
  - 7/04 0.07
  - 10/04 0.4
  - 4/05 0.8
  - 10/05 1.6

- What is the PSA DT of this patient?
  1. 3 mo
     • 6 mo
     • 9 mo
     • 12 mo
Case 1

MRI pelvis: No evidence of recurrence
Bone scan/ CXR: No evidence of metastases

What is the best treatment now?
1. Salvage RT
2. Salvage RT + 6 Mo hormone
3. Salvage RT + 24 Mo hormone
4. Salvage RT + Life long hormone
5. Observe
   • Hormonal treatment
Case 2

- American male aged 63 years old
- No underlying disease, KPI 90
- Presented w/ screening PSA 166.3 in Jan 2007
- PR exam showed normal prostate
- TRUS – Bx Oct/2007
- Patho: adenocarcinoma GS 3+3 in 6/6 cores rt and 6/6 cores lt.
Case 2

- MRI Pelvis: Diffuse heterogeneous low intensity T2WI with heterogeneous enhancement of the entire prostate. **Bilateral SV** involvement are observed.

- Bone scan: normal
Case 2

QUESTION 11

According to NCCN risk stratification, which risk group is this pt?

1. Low risk
2. Intermediate risk
3. High risk
4. Very high risk
Case 2

**QUESTION 12**

What treatment would you recommend for this patient?

1. Radical prostatectomy
2. Radiation therapy
3. Radiation + Hormonal therapy
4. Hormonal therapy alone
Case 2

What kind of hormone will you use for this patient?

1. LHRH agonist
2. LHRH antagonist
3. LHRH agonist + antiandrogen
4. LHRH antagonist + antiandrogen
5. Antiandrogen
Case 2

How long would you give hormonal therapy for this patient?

1. 6 mo
2. 12 mo
3. 24 mo
4. 36 mo
5. life long
**Hormonal Tx**
**combine w/ ERT**

<table>
<thead>
<tr>
<th>RCT Study</th>
<th>Pt criteria</th>
<th>Intervention</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>EORTC 22863</td>
<td>T3-4N0M0 or poorly diff (415)</td>
<td>LHRH D1 x 3 yr</td>
<td>Increase OS</td>
</tr>
<tr>
<td>RTOG 8531</td>
<td>T1-2N+ or T3 (945)</td>
<td>LHRH last wk ERT x continue</td>
<td>Increase OS only GS 8-10?</td>
</tr>
<tr>
<td>RTOG 8610</td>
<td>Bulky T2b-4Nx (471)</td>
<td>CAB neo x 2mo then concurrent</td>
<td>Increase OS only GS 2-6</td>
</tr>
<tr>
<td>RTOG 9202</td>
<td>T2c-4 (1554)</td>
<td>RTOG 8601 ± CAB 24 mo</td>
<td>Increase OS only GS 8-10</td>
</tr>
</tbody>
</table>
# Hormonal Tx

*combine w/ ERT*

<table>
<thead>
<tr>
<th>RCT Study</th>
<th>Intervention</th>
<th>5 yr Local control</th>
<th>5 yr distant control</th>
<th>5 Yr PSA control</th>
</tr>
</thead>
<tbody>
<tr>
<td>EORTC 22863</td>
<td>LHRH D1 x 3 yr</td>
<td>Increase &lt; .001</td>
<td>Increase &lt; .001</td>
<td>Increase &lt; .001</td>
</tr>
<tr>
<td>RTOG 8531</td>
<td>LHRH last wk ERT x continue</td>
<td>increase &lt; .0001</td>
<td>increase &lt; .0001</td>
<td>increase &lt; .0001</td>
</tr>
<tr>
<td>RTOG 8610</td>
<td>CAB neo x 2mo then concurrent</td>
<td>increase 0.016</td>
<td>increase 0.04</td>
<td>increase &lt; .001</td>
</tr>
<tr>
<td>RTOG 9202</td>
<td>RTOG 8601 + CAB 24 mo</td>
<td>Increase 0.0001</td>
<td>Increase 0.001</td>
<td>Increase 0.0001</td>
</tr>
</tbody>
</table>
# RT + H treatment for locally advanced prostate cancer

<table>
<thead>
<tr>
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<th>Pt criteria</th>
<th>Intervention</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>EORTC 22863</td>
<td>T3-4N0M0 or poorly diff (415)</td>
<td>LHRH D1 x 3 yr</td>
<td>Increase OS</td>
</tr>
<tr>
<td>RTOG 8531</td>
<td>T1-2N+ or T3 (945)</td>
<td>LHRH last wk ERT x continue</td>
<td>Increase OS only GS 8-10 ?</td>
</tr>
<tr>
<td>RTOG 8610</td>
<td>Bulky T2b-4Nx (471)</td>
<td>CAB neo x 2mo then concurrent</td>
<td>Increase OS only GS 2-6</td>
</tr>
<tr>
<td>RTOG 9202</td>
<td>T2c-4 (1554)</td>
<td>RTOG 8601 + CAB 24 mo</td>
<td>Increase OS only GS 8-10</td>
</tr>
<tr>
<td>EPC program</td>
<td>T1-4, anyN</td>
<td>Bicalutamide 150 mg after RT x continue</td>
<td>Increase OS, PSA RFS in LA T3-4 or N1</td>
</tr>
</tbody>
</table>
Zoladex adjuvant to RT significantly improves OS
EORTC 22863 at 5.5 years’ median follow-up

Bolla et al 2002

T1-2 of WHO grade 3 or T3-4 N0-1, M0 disease

Goserelin adjuvant to RT significantly reduced the risk of death by 49% compared with RT alone.
Zoladex adjuvant to RT significantly improves OS
RTOG 85-31 at 7.6 years’ median follow-up

HR 0.77 (p=0.001)

Goserelin adjuvant to RT significantly reduced the risk of death by 23% compared with RT alone

Goserelin + RT (n=488)
RT alone* (n=489)

Patients surviving (%)

Time since randomisation (years)

Pilepich et al 2005

cT3 disease or patients with regional lymphatic involvement
*Followed by observation and administration of goserelin at relapse
Casodex 150 mg adjuvant to RT significantly improves OS
EPC programme at 7.2 years’ median follow-up

McLeod et al 2006
T3-4, any N; or any N, T, N+ patients
Casodex 150 mg adjuvant to radiotherapy significantly improves survival

Locally advanced disease at 7.4 years’ median follow-up

In the RT group, numerically fewer patients receiving Casodex 150 mg died due to prostate cancer vs placebo (16.1% vs 24.3%)

Casodex adjuvant to radiotherapy: improves overall survival for locally advanced patients who wish to maintain their lifestyle
The OS benefits with Casodex and Zoladex were driven by a lower number of prostate cancer deaths

EPC programme\(^1\)
7.2 years’ median follow-up

RTOG 85-31\(^2\)
7.6 years’ median follow-up

<table>
<thead>
<tr>
<th>Prostate cancer mortality (%)</th>
<th>Bicalutamide 150 mg + RT</th>
<th>RT alone</th>
<th>Goserelin + RT</th>
<th>RT alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16%</td>
<td>24%</td>
<td>16%</td>
<td>22%</td>
</tr>
</tbody>
</table>

T3-4, any N, M0; or any T, N+, M0 patients
## Adverse Event: EPC program

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>No. patients (%)</th>
<th>Bicalutamide (n=694)</th>
<th>Placebo (n=664)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast pain</td>
<td>75</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Gynecomastia</td>
<td>67</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>16</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Hematuria</td>
<td>9</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Impotence</td>
<td>13</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>12</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Arthalgia</td>
<td>7</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Asthenia</td>
<td>13</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>
QUESTION 15

How confident you are for treatment of PC with hormonal therapy?

score 1-10

1 for minimal “I am not confident at all”

10 for maximal “I am very confident”
Thank you